

EXTRACTION OF *SWIETENIA MACROPHYLLA* SEED BY USING
MICROWAVE ASSISTED EXTRACTION TECHNIQUE AND THE
CHARACTERISATION OF ITS PHYTOCHEMICAL PROPERTIES

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DEDICATION

This thesis is dedicated to my parents,
Abu Bakar Bin Abdul Rahaman and Aminah Binti Ahmad

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ABSTRACT

Swietenia macrophylla (*S. macrophylla*) or commonly known as *Tunjuk Langit* in Malaysia has been used as traditional remedy for diseases treatment as the seeds of *S. macrophylla* have been examined for its anti-inflammatory, anti-mutagenicity, and anti-tumour activities. The objectives of this research are to optimise the extraction of the *S. macrophylla* seed oil by using microwave assisted extraction (MAE) and to evaluate physicochemical and biological properties of the extracted *S. macrophylla* seed oil. MAE provides process acceleration and higher extraction yield compared to conventional extraction. The operating parameters were optimized by response surface methodology using design expert version 6 to obtain optimum yield of *S. macrophylla* seed oil. Properties of *S. macrophylla* seed oil were characterised by using total phenolic content (TPC), antioxidant properties via DPPH (2,2-diphenyl-1-picrilhydrazyl) and ABTS (2,2'-azino-bis-(3-ethylbenzothiazoline-6-sulphonic acid)) free radical scavenging method, the anti-diabetic activity via α -glucosidase and α -amylase inhibition assays and the anti-microbial activity via agar disk-diffusion method. Gas chromatography-mass spectrometry (GC-MS) was used to analyse the fatty acid composition in the seed oil. The result showed that 43.69 ± 0.092 w/w % oil yield was obtained at optimal condition of 6 min irradiation time, solvent-to-solid ratio of 26 mL solvent/g solid and 460 W microwave power. The seed oil extracted by using MAE exhibited the highest TPC concentration, the best DPPH and ABTS inhibition compared to supercritical carbon dioxide extraction (SC-CO₂) and soxhlet extraction (SE) method. *S. macrophylla* seed oil demonstrated potent inhibition on α -amylase but weak inhibition towards α -glucosidase enzyme. *S. macrophylla* seed oil was found to have excellent inhibition zone towards *Escherichia coli* and *Bacillus subtilis*. Result from GC-MS analysis showed that the *S. macrophylla* seed oil was composed of fatty acids including linoleic (32.1%), oleic (57.3%) and palmitic (10.6%). These findings proved that *S. macrophylla* seed oil extracted using MAE could provide better quantity and quality of oil in shorter time compared to SC-CO₂ and SE methods.

ABSTRAK

Swietenia macrophylla (*S. macrophylla*) atau lazim dikenali sebagai *Tunjuk Langit* di Malaysia telah digunakan sebagai ubat tradisional untuk rawatan penyakit di mana biji *S. macrophylla* telah diperakui untuk aktiviti anti-radang, anti-mutagenisme, dan anti-tumor. Objektif penyelidikan ini adalah untuk mengoptimumkan pengekstrakan minyak biji *S. macrophylla* dengan menggunakan pengekstrak bantuan ketuhar gelombang mikro (MAE) dan untuk menilai sifat-sifat fizikokimia dan biologi daripada minyak biji *S. macrophylla* yang diekstrak. MAE menyediakan pecutan proses dan hasil ekstrak yang lebih tinggi berbanding dengan kaedah pengekstrakan konvensional. Parameter operasi dioptimumkan melalui kaedah permukaan tindak balas menggunakan *design expert* versi 6 untuk memperoleh hasil minyak biji *S. macrophylla* yang optimum. Sifat minyak biji *S. macrophylla* dikaji dengan menggunakan jumlah kandungan fenolik (TPC), sifat antioksidan menggunakan kaedah penyingkiran radikal bebas DPPH (2,2-dwifetil-1-pikrilhidrasil) dan ABTS (2,2-azino-bis (3-etilbenzothiazoline-6-asid sulfonik)), aktiviti anti-diabetes minyak biji dengan ujian perencatan enzim α -glucosidase dan α -amilase dan aktiviti anti-mikrob menggunakan kaedah resapan cakera agar. Kromatografi gas- spektrometri jisim (GC-MS) digunakan untuk menganalisa komposisi asid lemak bagi minyak biji tersebut. Keputusan menunjukkan sebanyak 43.69 ± 0.092 w/w% minyak telah dihasilkan pada keadaan optimum iaitu pada 6 minit masa penyinaran, nisbah pelarut kepada pepejal 26 mL pelarut/g pepejal dan 460 W kuasa gelombang mikro. Minyak biji yang diekstrak dengan menggunakan MAE menunjukkan kepekatan TPC tertinggi, perencatan DPPH dan ABTS terbaik berbanding pengekstrakan karbon dioksida superkritikal (SC-CO₂) dan pengekstrakan kaedah soxhlet (SE). Minyak biji *S. macrophylla* menunjukkan perencatan yang kuat terhadap enzim α -amilase tetapi lemah terhadap enzim α -glucosidase. Minyak biji *S. macrophylla* didapati menghasilkan zon perencatan yang baik terhadap *Escherichia coli* dan *Bacillus subtilis*. Hasil daripada analisis GC-MS mendapati bahawa minyak biji *S. macrophylla* terdiri daripada beberapa asid lemak termasuk linoleik (32.1%), oleik (57.3%) dan palmitik (10.6%). Penemuan ini membuktikan bahawa minyak biji *S. macrophylla* yang diekstrak menggunakan MAE dapat memberikan kuantiti dan kualiti minyak yang lebih baik dalam masa yang lebih singkat berbanding kaedah SC-CO₂ dan SE.

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LIST OF ABBREVIATIONS

<i>S. macrophylla</i>	-	<i>Swietenia macrophylla</i>
<i>S. humilis</i>	-	<i>Swietenia humilis</i>
<i>S. condollie</i>	-	<i>Swietenia condollie</i>
<i>S. mahagoni</i>	-	<i>Swietenia mahagoni</i>
PUFA	-	Polyunsaturated Fatty Acid
CVD	-	Cardiovascular Disease
SE	-	Soxhlet Extraction
SC-CO ₂	-	Supercritical Carbon Dioxide Extraction
MAE	-	Microwave Assisted Extraction
RSM	-	Response Surface Methodology
TPC	-	Total Phenolic Content
DPPH	-	2,2-diphenyl-1-picrylhydrazyl
ABTS	-	2,2'-azino-bis-(3-ethylbenzothiazoline-6-sulphonic acid)
GC-MS	-	Gas Chromatography Mass Spectrometry
GC	-	Gas Chromatography
STZ	-	Streptozotocin
SFE	-	Supercritical Carbon Dioxide Extraction
UAE	-	Ultrasound-Assisted Extraction
ASE	-	Accelerated Solvent Extraction
CO ₂	-	Carbon dioxide
CHSE	-	Conventional Heating-Stirring Extraction
MAAEE	-	Microwave Assisted Enzymatic Extraction
UMAE	-	Ultrasonic-Microwave Assisted Extraction
NMAE	-	Negative Pressure Cavitation–Microwave Assisted
SWE	-	Subcritical Water Extraction
HPLC	-	High Performance Liquid Chromatography
H ₂ O	-	Water
DMSO	-	Dimethyl sulfoxide
WHO	-	World Health Organization
FRIM	-	Forest Research Institute Malaysia

LIST OF SYMBOLS

°C	-	Degree celcius
μm	-	Micrometer
h	-	Hour
mg	-	Milligram
g	-	Milligram
mL	-	Millilitre
min	-	Minute
W	-	Watt
a_{ij}	-	constant regression coefficients
MPa	-	Megapascal
mm	-	Millimetre
R^2	-	Determination coefficient
Adj R^2	-	Adjusted determination coefficient

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CHAPTER 1

INTRODUCTION

1.1 Background of the Study

Swietenia macrophylla (Linn.) Jacq. (Meliaceae) grows and multiply mostly in tropical areas of Asia, including India, Malaysia, Indonesia and southern mainland China (Orwa et al., 2009) but the breed came from Bahamas, Cuba, Haiti, Jamaica, Netherlands Antilles, and United States of America. There are other species in the same group including *S. humilis*, *S. condollie* and *S. mahagoni*. The bark of *S. macrophylla* is known as astringent for the remedy for diarrhoea, as supplements, and as haemorrhage inducer. It also aids to clear blood, healthy appetite, and strength revival for disease such as tuberculosis by using ream liquid soaked bark (Orwa et al., 2009). Meanwhile, the seed has been used as anti-hyperglycaemic drug, body ointment to enhance the healing of skin cuts, itches and wound (Naveen et al., 2014) and has decent antioxidative effect (Kanti et al., 2013). It also has been investigated for its capability to serve as inflammatory prevention, tumour prevention activities and mutagenicity prevention (Guevara et al., 1996). *S. macrophylla* or commonly known as *Tunjuk Langit* in Malaysia has been used as traditional remedy for diseases treatment such as diabetes. Previous research by Hashim et al. (2013) has stated that fucosterol and β -sitosterol might be the responsible bioactive compounds to serve as antidiabetic agent while Koba & Yanagita (2013) has proved linoleic acid to exhibit the same potential.

Diabetes is a chronic condition when glucose remains circulating in the blood stream due to the lacking and ineffectiveness of the insulin in the body. The function of insulin is to transport glucose from blood stream into cell to be used as energy (McLaughlin et al., 2015). Diabetes mellitus occurs when there are defects either in insulin secretion, insulin action or both. There are 3 types of diabetes mellitus including Type 1, Type 2 and gestational diabetes. Type 1 diabetes is caused by the damage of β -cells of the pancreas which result in decreased insulin supply to the

circulation. The patients need to fully depend on insulin injection on daily basis while Type 2 results in peripheral insulin resistance, thereby results in decreased insulin sensitivity to the skeletal muscles, adipose tissues and liver. There are a lot of other factors such as aging, obesity, physical inactivity, population growth and urbanization that can lead to steady increase diabetes sufferers (Choudhury et al., 2018). The last category of diabetes is gestational diabetes which commonly occur to pregnant woman and normally disappears after birth.

Statistically, the diabetes sufferer total number is expected to increase from 414.7 million in 2015 to 641.7 million in 2040. China is the first country with the greatest number of adults with diabetes followed by India and United States of America (USA) (McLaughlin et al., 2015). Meanwhile in Malaysia, there were over 3 million cases of diabetes in 2017 (World Health Organization, 2016). In USA, more than 90% of diabetes patients suffered from Type 2 diabetes and affected 9.3% of USA population. Adults diagnosed with diabetes treat the disease by oral medication (56.9 %), insulin (14 %), both (14.7 %), and 14.4 % use neither (Tran et al., 2015). Oral medicine was acknowledged as the major treatment for diabetes. However, commercial antidiabetic drugs such as sulfonylureas and rosiglitazone have been reported to have side effects such as increased risks of cardiovascular disease (CVD) and stroke (Castilla-guerra et al., 2018). Therefore, the search in natural sources for antidiabetic drugs should be taken seriously to provide an alternative to the patients.

Plants contain bioactive compounds, which are secondary plant metabolites responsible to provide pharmacological or toxicological benefits in human body (Bernhoft, 2010). Secondary metabolites derived from fatty acids such as omega-3 and omega-6 fatty acids are called essential fatty acids because cannot be made by the body in desired amounts, so they must be consumed in the diet. omega-3 polyunsaturated fatty acids (PUFA) was derived from original fatty acid α -linoleic acid while omega-6 PUFAs were derived from linoleic acid (Corte et al., 2018). Nutritional studies in animal models have shown loads of advantageous health effects by consuming conjugated linoleic acid including anti-obesity, anticarcinogenic and antidiabetic effects. Previous research has reported that

S. macrophylla contains linoleic acid as major composition of fatty acid with 33.87% and 49.08% for plant origin from India and Mexico respectively (Chakrabarty and Chowdhuri, 1956). This information supported that *S. macrophylla* seed oil can be a good source of PUFA for diabetes Type 2 treatment.

In order to prepare oral medication to treat diabetes, a good extraction method to produce optimum oil yield should be studied to extract optimum bioactive compound that can contribute to the treatment process (Tran et al., 2015). The extraction method is divided into two categories which are conventional method and modern method. Conventional extraction method such as Soxhlet extraction (SE) is widely used since 1879, however, it has many downsides compared to other extraction method because it uses long time for extraction process and huge amount of extractant which also leads to environmental problem as it is expensive to dispose. The thermolabile of targeted species might also be decomposed due to exposure to high temperature for long time. Soxhlet extraction method also limited by extractant and no automation process (Castro and Priego-Capote, 2010). Meanwhile, for supercritical carbon dioxide extraction (SC-CO₂), it is a rising modern method for extraction which provide shorter time and automated process. Nevertheless, it also has disadvantages such as not suitable for samples containing high amounts of water, low yield of polar compound and it is a high cost instrumentation (Khaw et al., 2017).

Another promising modern extraction method is microwave assisted extraction (MAE) which provides environmentally friendly automated process. In comparison with SC-CO₂, it provides higher extraction efficiency, reduction of solvent usage about 90%, shorter time, high sample amount, low cost and easier to handle (Calle & Costas-Rodríguez, 2017). Even though the biggest concern with MAE is the loss of bioactive compound due to the exposure to the irradiation, this problem can be overcome with intermittent microwave extraction process. Intermittent extraction prevents samples from overheating while balancing heat, mass transfer processes and improves the efficiency of bioactive compounds extraction (Swamy and Muthukumarappan, 2017).

S. macrophylla was chosen in this study because it has higher total phenolic content compared to seed oil of blueberry, red raspberry, marionberry and boysenberry which have much lower TPC which ranges from 0.9 to 2 mg GAE/mg. (Parry et al., 2005). According to Moghadamtousi et al. (2013), *S. macrophylla* has exceptional advantages in phytomedicine because of the diversity in biological activities including antimicrobial, anti-inflammatory, antioxidant effects, antimutagenic, anticancer, antitumor and antidiabetic activities. This study aims to optimise the extraction of *S. macrophylla* seed oil by using microwave-assisted extraction with three main parameters which were time, microwave power and solvent to solid ratio to give the best yield of oil. Characterisation of optimum extract from different methods including SE, SC-CO₂ and MAE were performed to compare the properties of the extract in order to evaluate advantages and disadvantages of each method. The oil extracted at optimum conditions was subjected to antioxidant, antimicrobial and antidiabetic test to prove the ability of the extract to serve as an alternative for diabetes treatment. *In vitro* diabetic model was used to analyse the antidiabetic activities. In addition, the correlation of linoleic acid and the inhibitory activities of α -glucosidase and α -amylase were also investigated.

1.2 Problem Statement

In 2011, there were approximately 366 million people suffered diabetes mellitus and the number is expected to increase to 439 million by 2030. Type 2 diabetes mellitus sufferers in low and middle income country has been increasing by 80% and caused 4.6 million deaths in 2011 (Olokoba et al., 2012). There were over 3 million cases of diabetes in Malaysia in 2017 (World Health Organization, 2016). The exploration for brand new drugs continues even with considerable development in treatment by using oral hypoglycaemic agents because the existing synthetic drugs have several limitations (Issa & Bule, 2015) and adverse effects (Patel et al., 2012) such as hypoglycaemia, liver damage, gastrointestinal symptoms, and weight gain (Eleazu et al., 2018). Hence, it is crucial to develop a safe and effective treatment for diabetes. Plants offer excellent option to cure diabetes by providing safe and effective medication because plants have been an exemplary source of medicine since ancient times. Herbal plants have been traditionally used for diabetes treatment

worldwide. Plant drugs are frequently considered to be less toxic and free from side effects than synthetic drugs (Patel et al., 2012). In this case, *S. macrophylla* has been proven by previous studies to have the ability to serve as the cure for many diseases such as diabetes mellitus (Jemain et al., 2011), hypertension and malaria (Dewanjee and Maiti, 2011). There are a number of bioactive compounds that reckoned to contribute as antidiabetic agent such as fucosterol, β -sitosterol (Hashim et al., 2013), and linoleic acid (Hartati et al., 2018)

Appropriate and standardised extraction techniques with optimum oil yield recovery are needed in order to obtain bioactive compounds from plant materials for isolation, identification, characterisation and industrial production purposes (Reinoso et al., 2017). The growing attention in plant secondary metabolites is followed by a need to develop and modify the resource of plant extraction protocols. However, the conventional extraction process may require high cost and long extraction time such as Soxhlet method, which has the drawbacks of using huge volume of solvent and prolonged extraction time of compounds producing lower yield. The increasing demand of herbal products requires wider, safer and high quality production with low processing cost and higher yield in order to grow herbal and nutraceutical medicine based industries (Belwal et al., 2018). To achieve these expectations, an increased demand for alternative and modern extraction process have been introduced such as microwave assisted extraction (MAE) and supercritical carbon dioxide extraction (SC-CO₂). MAE has the ability to efficiently extract multiple samples simultaneously in short time (about 90% time reduction), low cost and minimal usage of solvent volume (Dean and Tyne, 2012). MAE also has promising advantages against SC-CO₂ which is easier to handle, lower cost equipment and provide higher extraction yield in shorter extraction time. It is also appropriate for thermolabile constituents and offers agitation during extraction to improve the mass transfer phenomenon (Mandal and Siva, 2006).

1.3 Objectives of the Study

This study aimed to achieve the following objectives:

- a) To optimise the extraction of the *S. macrophylla* seed oil by using microwave-assisted extraction (MAE).
- b) To evaluate physicochemical and biological properties of the extracted *S. macrophylla* seed oil.

1.4 Scope of the Study

In order to achieve the objectives stated in section 1.3, the scopes of study were as follows:

- i. Optimisation of *S. macrophylla* extraction using MAE was performed by using Response Surface Methodology (RSM) at three parameters, which were time (3, 5 and 7 min), solvent to solid ratio (10, 20 and 30 mL/g) and microwave power (300, 400 and 500 W) using seed oil yield as the response.
- ii. Extraction of *S. macrophylla* seed oil was performed at optimum conditions according to previous research using SE with solvent to solid ratio 50:1, ethanol as solvent and 6 h extraction time (Mohan et al., 2016) and SC-CO₂ with 710 µm particle size, temperature 67.88°C and pressure at 29.02 MPa (Hartati et al., 2018) .
- iii. Characterisation of the oil extracted from SE, SC-CO₂ and MAE at optimum conditions using total phenolic content (TPC) and antioxidant assays including DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging activity and ABTS (2,2'-azino-bis-(3-ethylbenzothiazoline-6-sulphonic acid)) radical cation decolorisation assay. Investigation on *in vitro* study of antimicrobial activity of *S. macrophylla* oil was conducted by using disk diffusion assay by

using *Escherichia coli* as gram negative and *Bacillus subtilis* as gram positive and *in vitro* study of antidiabetic activity of *S. macrophylla* oil was analysed by α -amylase and α -glucosidase enzymes inhibition assays. Linoleic acid content was evaluated by using Gas Chromatography Mass Spectrometry (GC-MS) analysis.

1.5 Significance of the Study

- i. The data obtained from the optimised extraction of *S. macrophylla* seed oil by using microwave assisted extraction would be very useful because there is no extraction of *S. macrophylla seed* oil by using microwave assisted method yet. It is important to always seek for new alternative method to enhance the extraction method and produce better yield quality.
- ii. The study of antidiabetic property of *S. macrophylla* seeds using α -amylase and α -glucosidase enzymes inhibition assays can be contributed in the pharmaceutical and nutraceutical industries.
- iii. The correlation between linoleic acid content in the oil extract and the antidiabetic activities is important to prove that linoleic acid is one of the major contributing bioactive compounds towards antidiabetic activities.

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